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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,660	09/15/2005	Jean-Louis Junien	102717.58257US	9879

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EXAMINER

ROBERTS, LEZAH

ART UNIT	PAPER NUMBER
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1612

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/536,660	Applicant(s) JUNIEN ET AL.	
	Examiner LEZAH W. ROBERTS	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-18, 20 and 21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-17, 18, 20 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to the Amendment filed April 16, 2008. All previous rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 102 – Anticipation (Previous Rejection)

Claims 12-13, 15-17 were rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al. (US 2003/0092736). The rejection is maintained and further applied to claims 18, 20 and 21.

Applicant's Arguments

Applicants assert Cheng et al. fail to teach, or suggest, Applicants' ditherapy, a method for treating obesity by treating a patient with a pharmaceutical composition consisting of metformin and the particular PPAR α agonists recited in Applicants' claims. Therefore it does not disclose each and every limitation of a claimed invention and fails to anticipate Applicants' invention. In contrast, Cheng et al. teach the administration of their new azole acid derivatives, alone or in combination with anti-diabetic and/or anti-lipidemic agents and other therapeutic agents. Cheng et al. disclose lists of many possible combinations of many agents to treat many different diseases and contain numerous paragraphs disclosing lists of therapeutic agents that could be used, always

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in association with the new azole acid derivatives of the invention. A general disclosure of various compounds always in combination with Cheng's azole acid derivatives does not anticipate the use of the particular combinations recited in Applicants' claims or the synergistic effect of metformin in combination with the fibrates (see Table 3) to treat a specific disease (*viz* obesity). Applicant further asserts that unexpected results were seen when measuring triglyceride levels (See Remarks filed April 16, 2008).

Examiner's Response

The claims recite the language "comprising" and therefore the method of treatment may include other compounds other than metformin and fenofibrate. Although the reference disclose lists, in regards to the anti-diabetic agent, it names only two specifically, one being metformin. The reference also specifically names fenofibrate as a choice that may be used as a lipid lowering agent in combination with the anti-diabetic agent. Therefore the reference strongly suggests using these two compounds in combination. In regards to the synergistic effect, Applicant's data from Table 3 appear to be additive effects based on the error of the values. There appears to be some overlap between the fenofibrate body weight and the fenofibrate plus metformin body weight, where both encompass 48 grams. In regards to Table 2, the individual values for T0 and T15 appear additive when comparing the first 4 values. It is difficult to determine if there is any synergistic effect based on the percentages because the percentages are ratios and are reflective of the numbers for T0 and T15 and not really the change in T0 and T15 values.

Claim Rejections - 35 USC § 103 – Obviousness (Previous Rejections)

1) Claims 12-17 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (Obesity Research 1998) in view of Chaput et al. (Biochemical and Biophysical Research Communications 2000). This rejection is maintained and further applied to claims 18, 20 and 21.

Applicant's Arguments

Applicants respectfully disagree and argue Chaput does not compensate for Lee's deficiencies. Chaput discloses the effect of fenofibrate and rosiglitazone on lowering serum triglycerides with opposing effects on body weight. Results presented by Chaput show that fenofibrate decreases body weight gain in fatty Zucker rats but, "[t]he cited art must be considered for all that it teaches, and the Examiner is not permitted to pick and choose from those teachings only so much that would render the claims obvious." ATD Corp. v. Lydall, Inc. 48 USPQ2d 1321 (Fed. Cir. 1998). Chaput also teaches against fenofibrate having any effect on weight gain in Sprague Dawley rats. Chaput discloses that previous reports teach that fenofibrate does not affect body weight in Sprague Dawley rats. Such conflicting results teach away from using fenofibrate for treating obesity. Thus one of skill in the art would not be motivated to particularly combine fenofibrate, or any of the other particular PPAR α agonists recited in Applicants' claims, with metformin. Furthermore, one of skill in the art in view of Lee in combination with Chaput would have no reason to expect that fenofibrate in

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combination with metformin would have a synergistic effect on weight loss. See Cheng et al. above in regards to unexpected results reported in Table 2 and 3.

Examiner's Response

Chaput teaches fenofibrate causes weight loss in rats. The disclosure that in a previous study fenofibrate did not cause weight loss is not teaching away because they were different types of rats. The rats used in the reference of Chaput are rats used as a diabetic model and therefore the results may be more pertinent to the metabolic situation that exists in the diabetic patient (page 448, col. 2). It would therefore be obvious to combine the references because both the disclosed compounds are used by diabetics and it would be obvious to one of skill in the art to use them in combination for those diabetic patients needing to lose weight. The claims are not directed to certain types of individuals and therefore the reference is not teaching away from obese individuals with diabetes. In regards to the synergistic effect, Applicant's data from Table 3 appear to be additive effects based on the error of the values. There appears to be some overlap between the fenofibrate body weight and the fenofibrate plus metformin body weight, where both encompass 48 grams. In regards to Table 2, the individual values for T0 and T15 appear additive when comparing the first 4 values. It is difficult to determine if there is any synergistic effect based on the percentages because the percentages are ratios and are reflective of the numbers for T0 and T15 and not really the change in T0 and T15 values.

2) Claims 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (Obesity Research 1998) in view of Piomelli et al. (US 2005/0101542). This rejection is maintained and further applied to claims 18, 20 and 21.

Applicant's Arguments

Applicant argues Piomelli does not compensate for Lee's deficiencies. Piomelli is related to pharmaceutical use of a combination of PPAR α agonists and a CB1 cannabinoid receptor antagonist to reduce excess or unwanted appetites for consumption of appetizing substances, such as foods, alcohol, and psychoactive substances of abuse. While a method for treating or preventing obesity or overweight by administering a combination providing both a cannabinoid CB1 receptor antagonist and a PPAR α agonist is mentioned, such a disclosure is insufficient to motivate one of skill in the art to combine the particular Markush group of PPAR α agonists recited in the instant claims with metformin in a method to treat obesity because metformin is not an antagonist of the cannabinoid CBI receptor, and thus one of skill in the art, would not be motivated to use metformin with Piomelli's assays. Furthermore, Piomelli simply provides a laundry list of compounds including, among others, clofibrate, fenofibrate, bezafibrate, gemfibrozil and ciprofibrate. The inventors themselves indicate that clofibrate alone does not inhibit food intake, whereas other PPAR α agonists, such as Wy-14643 and GW7647, do (see [0429]). Accordingly, Piomelli's disclosure does not teach or suggest that the fibrates in combination with a cannabinoid CB1 receptor

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antagonist are effective in treating or preventing obesity. Thus one of skill in the art based on the teachings of Piomelli, would not be motivated to combine Piomelli with Lee and use metformin in combination with the particular PPAR α agonist recited in Applicants' claims. See Cheng et al. above in regards to unexpected results reported in Table 2 and 3.

Examiner's Response

Piomelli et al. does not just mention methods to treat obesity, it discloses that the present invention meets the need for treating obesity and overweight. This would lead one to believe that this is a main objective of the reference. The claims recite the language "comprising" and therefore the method of treatment may include other compounds other than metformin and fenofibrate. Therefore there is nothing in Applicant's claims that excludes one of skill in the art from using a cannabinoid receptor antagonist in combination with the compounds recited in the instant claims. The reference specifically names fenofibrate as being an agent that may be used in the disclosed methods. It would have been obvious to one of ordinary skill in the art to have combined the compositions comprising fenofibrate and a cannabinoid receptor antagonist with metformin motivated by the desire to use compounds that have been used to aid in weight loss in order to improve weight loss results and to improve treatment of diabetes when the patient suffers from the symptom due to weight, as supported by In re Kerkhoven, as cited in the previous office action, especially if the compositions have different mechanisms of action. This is beneficial by treating the

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different causes of symptoms of obesity. In regards to the synergistic effect, Applicant's data from Table 3 appear to be additive effects based on the error of the values. There appears to be some overlap between the fenofibrate body weight and the fenofibrate plus metformin body weight, where both encompass 48 grams. In regards to Table 2, the individual values for T0 and T15 appear additive when comparing the first 4 values. It is difficult to determine if there is any synergistic effect based on the percentages because the percentages are ratios and are reflective of the numbers for T0 and T15 and not really the change in T0 and T15 values.

3) Claims 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (US 2002/0173663). This rejection is maintained and further applied to claims 18, 20 and 21.

Applicant's Arguments

Applicants argue Liu provides laundry lists of many compounds and possible combinations of compounds and many diseases that might be treated. Such a disclosure is insufficient to motivate one of skill in the art to combine the particular PPAR α agonists with metformin as recited in the instant claims. And, one of skill in the art would have no reason to expect that their combination would produce the synergistic effect disclosed in Applicants' specification. As such, Liu does not render Applicants' invention obvious. See Cheng et al. above in regards to unexpected results reported in Table 2 and 3.

Examiner's Response

Although the reference discloses a laundry list of compounds leading to various combinations, absent of unexpected results, it would have been obvious to one of ordinary skill in the art to have used the metformin and fenofibrate in combination based on the disclosure that they may be used in combination and are specifically named by the reference to treat conditions such as obesity. In regards to the synergistic effect, Applicant's data from Table 3 appear to be additive effects based on the error of the values. There appears to be some overlap between the fenofibrate body weight and the fenofibrate plus metformin body weight, where both encompass 48 grams. In regards to Table 2, the individual values for T0 and T15 appear additive when comparing the first 4 values. It is difficult to determine if there is any synergistic effect based on the percentages because the percentages are ratios and are reflective of the numbers for T0 and T15 and not really the change in T0 and T15 values.

Claims 12-18, 20 and 21 are rejected.

No claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **LEZAH W. ROBERTS** whose telephone number is (571)272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lezah W Roberts/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612